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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
09/337,756	06/22/99	HANSEN	H 018733/0884

HM12/0220

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EXAMINER	
SAUNDERS, D	
ART UNIT	**PAPER NUMBER**
1644	10

DATE MAILED: 02/20/01

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 11/22/00.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1-50 is/are pending in the application.

Of the above, claim(s) 35-50 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 1-34 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☑ Claims 1-50 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4, 5, 7

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

-- SEE OFFICE ACTION ON THE FOLLOWING PAGES --

★ U.S. GPO: 1996-410-238/40050

Claims 1-50 are pending.

Applicant's election without traverse of Group I (claims 1-34) in Paper No. 9, filed on 11/22/00, is acknowledged.

The drawings are objected to because figure 3, as filed, has left out the "l" of "light chain" recited to the left of construct A. Correction is required.

The disclosure is objected to because of the following informalities: the current status of various copending applications referenced in the specification (e.g. pages 26, 27, 29) must be updated.

Appropriate correction is required.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

The sequences recited, for example, at specification pages 12-13 and 38 have backbones with 4 or more amino acids which are not D amino acids and hence fall within the scope of sequences encompassed by 37 CFR 1.821-1.825.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-4, 6-10, 12-20, 25-27, 30, 32-34 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-21 and 25-28 of copending Application No. 09/382,186. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 5, 11, 21-24, 28-29 and 31 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 and 25-28 of copending Application No. 09/382,186. Although the conflicting claims are not identical, they are not patentably distinct from each other because while the agents of instant claims 5 and 11, the peptides of instant claims 21-24, and the chelators of instant claims 28-29 are not recited in the copending claims, these features are all disclosed in the copending specification. Therefore these specific limitations are all clearly encompassed by copending generic claim 1, and issuing one application sans disclaiming over the other would lead to an undue extension of patent rights. The kit of instant claim 31 is not recited in the copending claims; however, the method using the kit components is recited in copending claim 2, and provision of these components in a kit would have been obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 16-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 16-19 it is unclear what the respective "peptide", "carbohydrate", "hapten" or "chelator" is in relation to the conjugate defined in independent claim 1. Is each of these the carrier, the epitope, or some other portion of the conjugate? Dependent claims 20-29 are included in the rejection.

In claim 28 "said soft base chelator" lacks antecedent basis. Does applicant intend this claim to depend from 25?

Prior to examination over the prior art, the examiner notes that the instant claims are only given benefit of the instant filing date of 6/22/99. The examiner finds no description of the instant invention comprising bispecific antibody with one arm reactive with a target tissue and the other arm reactive with a targetable conjugate, via binding of the other arm to an epitope of the conjugate. Provisional applications 60/104,156 and 60/090,142 disclosed the other arm as being reactive with a linker moiety, rather than an epitope of a conjugate. Since the former concept is narrower in scope than the latter, the claims are properly only given benefit of the instant filing date.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Claims 1, 9, 16, 18-19, 32 and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Bardies et al. (J. Nucl. Med. 37, 1853, 1996, submitted as ref. A9 with Paper No. 5).

Bardies et al. show a bispecific monoclonal antibody with one arm to In-DTPA. These are precisely the specificities of the bispecific antibodies shown by applicant in the embodiments of Examples 17 and 21 and employed in the pretargetting experiments of Examples 24. Also, note specification page 10 teaching DPTA as a hapten. Hence, the bispecific antibody of claims 32 and 34 by applicant was known in the art. The instant limitation that the other arm "binds a targetable conjugate" lends no patentable weight to the claim, since binding to a conjugate represents an intended use by applicant, and the binding of the prior art bispecific antibody to In-DTPA would inherently be directed to an In-DTPA hapten component of a targetable conjugate.

With respect to the method claims, Bardies et al. show administration of the above noted bispecific antibody, followed by administration of the conjugate di-DTPA-TL in a diagnostic agent (claim 19), containing peptide bond (claim 16), hapten moiety (claim 18) and chelator (claim 19). The antibodies of each arm of the bispecific antibody are monoclonal (claims 12-13).

Claims 1, 9, 16, 18-20, 32 and 34 are rejected under 35 U.S.C. 102(a) as being anticipated by Gautherot et al. (J. Nucl. Med. 39: 1937, 1998, ref A 7 of Paper 5).

With respect to antibody claims 32 and 34, Gautherot et al. show the same bispecific antibody as that of Bardies et al. noted supra. Regarding the method claim, Gautherot et al. also show a method like that of Bardies et al., with the additional feature that the bispecific antibody is radiolabelled with iodine 125 or 131, as in instant claim 20.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 30 is rejected under 35 U.S.C. 102(a) or (b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Gautherot et al. or Bardies et al., respectively.

The above discussed references show all kit components. As a mere collection of these, the kit is anticipated. If the term "kit" is considered as implying packaging, such was conventional in the art and would have been obvious for the sake of conveniently providing the components.

Note, numerous publications submitted by applicant other than Bardies et al. or Gautherot et al. could have been cited for showing the bispecific antibody and method. For the sake of brevity the examiner has only cited these.

Claims 1, 3, 9, 12-16, 18-19, 24-29 and 32-34 are rejected under 35 U.S.C. 102(a) as being anticipated by Karacay et al. (Proceedings ... 40, 644, 1999, supplied as ref AS with Paper 5).

Karacay et al. show a monoclonal, humanized bispecific antibody directed to CEA and In - DPTA--i.e. the arms have the same specificities as the monoclonal bispecific antibody of Bardies et al. cited supra against claims 32 and 34. Karacay et al. show the instant method of claim 1. They teach radioimmunodetection and radio immunotherapy, as in claims 3 and 9.

They teach use of a targetable conjugate (IMP 192) which has all features recited in instant claims 16, 18-19 and 24-29.

Claim 30 is rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Karacay et al. (Proceedings...).

Karacay et al. show all components of the kit of claim 30. As a mere collection of components the kit is anticipated. If weight is given to the term "kit" as implying packaging, such was conventional in the art and would have been obvious for the sake of conventional in the art and would have been obvious for the same of conviently providing the components needed to conduct the taught imaging and/or therapeutic methods.

Claims 1, 3, 9, 12-16, 18-19, 24-30 and 32-34 are rejected under 35 U.S.C. 102(a) as being anticipated by Karacay et al. (J. Nuc. Med. 40, No. 5 suppl. p. 255, 1999, suppled as ref. A6 with Paper 7).

Karacay et al. (J. Nuc. Med.) have essentially the same disclosure as Karacay et al. (Proceedings...) discussed supra, and show, also, the feature of a kit.

The examiner notes that the above cited references of Bardies et al., Gautherot et al. and Karacay et al. (Proceedings ... and J. Nucl. Med.) use a bispecific antibody with one arm directed to the In-chelator. Applicant appears to teach away from this in the paragraph spanning specification pages 11-12, but then uses a bispecific antibody with the same specificities as the antibodies of the prior art in specification Example 24. Thus the examiner considers it proper to have cited these references. Clarification as to the nature of the invention is requested.

Claims 1, 3, 6-7, 9-10, 12-13, 16, 18-19, 32 and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Barbet et al. (EP 0,263,046, supplied as re A3 with Paper 5).

Barbet et al. show bispecific antibodies with a first arm directed to a target antigen on a cell and a second arm directed to a hapten component of a conjugate comprising one or more copies of the hapten and "effector" (i.e. therapeutic or diagnostic agent) group. The antibody arms in each case are taught as monoclonal (page 4, lines 50-65). Thus all features of composition claims 32 and 34 are taught.

Barbet et al. teach a method in accord with instant claim 1. See page 6, lines 38-55. They teach therapeutic and imaging agents in accord with instant claims 3 and 9. See page 5, lines 27-35 and page 6, lines 40-45. Also, they disclose toxins and drugs, as in instant claims 6-7. See page 5, lines 46-50. The conjugates can contain peptide structures, in accord with instant claim 16. See page 5, lines 41-43. Barbet et al. teach paramagetic labels, which would have immediately led one to envision MRI, in accord with instant claim 10. See page 5, lines 36-43.

Claim 30 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Barbet et al. (EP 0,263,046).

While Barbet et al. do not expressly teach a kit, such is considered anticipated or obvious for reasons noted supra regarding Bardies et al.

Claims 1, 3, 6-7, 9, 12-13, 18-19, 30, 32 and 34 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Goodwin et al. (4,863,713).

Goodwin et al. show a method involving administration of a "binding protein", followed by a "clearing agent", followed by an "epitopic compound". See col. 10, line 10 - col. 12, line 10, for example. The "epitopic compound" can include one or more hapten moieties, which are binding partners for an antibody, linked to an therapeutically active agent or imaging agent. See col. 4, line 55- col. 7, line 6. This "epitopic compound" corresponds to the targetable conjugate of instant claims 1 and 30, part C) of each. The "binding protein" can be comprised of monoclonal, bispecific antibodies, with one arm directed to a target tissue and the other arm directed to the epitopic compound. See col. 7, line 8 - col. 9, line 36, especially at col. 9, lines 3-36. This "binding protein" corresponds to the bispecific antibody of claims 1 and 30, part (A) of each. Thus the bispecific antibody of claims 32 and 34, as well as the method of claim 1 and components of the kit of claim 30 are shown.

Regarding dependent claims 3, 6-7, 9, and 19 note the therapeutic and imaging agents taught at col. 5, lines 1-19.

Claims 1, 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barbet et al. or Goodwin et al., either in view of Griffiths (6,187,284).

Barbet et al. and Goodwin et al. have been cited supra against claims 1 and 9. The feature of performing PET, as recited in further dependent claim 9, was known in the art, as shown by Griffiths in the methods of Barbet et al. or Goodwin et al. would have been obvious.

Claims 1, 14-15, and 32-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bardies et al, Gautherot et al., Barbet et al., or Goodwin et al., any in view of Goldenberg (WO 96/04313, re A2 of Paper 5).

Each of the primary references, teaching murine bispecific antibodies, has been cited supra against claims 1 and 32. Goldenberg teaches (pages 6, 18 and 21) that use of humanized antibodies is known for the targetting of therapeutic or imaging agents. It would have been obvious to humanize the bispecific antibodies of the primary references, since Goldenberg teaches that this avoids problems associated with the immunogenicity of murine antibodies (page 21).

Claims 1 and 4-5 are provisionally rejected under 35 U.S.C. 103(a) as being obvious over copending Application No. 09/205,243 which has a common invention with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e) if patented. This provisional rejection under 35 U.S.C. 103(a) is based upon a presumption of future patenting of the conflicting application. Barbet et al. and Goodwin et al. have been cited further supra. Copending application '243 shows that use of boron - 10 enriched isotopes to effect BNCT was conventional in immunotherapy. It hence would have been obvious to employ such a therapeutic agent in the methods of Barbet et al. or Goodwin et al.

This provisional rejection might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the

inventor of this application and is thus not the invention "by another," or by a showing of a date of invention for the instant application prior to the effective U.S. filing date of the copending application under 37 CFR 1.131.

Claims 1 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barbet et al. or Goodwin et al. either in view of Kondratyev (5,502,037).

Barbet et al. and Goodwin et al. have been cited supra against claim 1 for teaching the use of bispecific antibodies directed against a targetting component of a therapeutic agent - hapten conjugate. Kondratyev shows that prodrugs can be targetted by monoclonal antibodies to internalizable antigens on target cells, such that the prodrug will be internalized and converted by the target cell into an active drug. See col. 5, line 55+. Since the methods of Barbet et al. and Goodwin et al. are taught as modifications/improvements over methods that employ antibody targetting of directly conjugated therapeutic agents (as in the case of Kandratyev) it would have been obvious to provide the hapten moieties, taught by Barbet et al. or Goodwin et al., conjugated to the prodrug of Kondratyev, and to use these conjugates with bispecific antibodies.

Claims 1 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barbet et al. or Goodwin et al., either in view of Huston et al. (5,534,254).

The primary references have been cited supra against independent claim 1, regarding dependent claim 20; Huston et al. show the further feature (cols. 6-7) of providing a radioisotope on a bispecific antigen and a therapeutic agent. This provision of a radioisotope permits the imaging of cells expressing the target antigen or the destruction of such cells. To gain either of

these advantages it would have been obvious to provide such a radioisotope on the bispecific antibodies of Barbet et al. or Goodwin et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, Ph.D. whose telephone number is (703) 308-3976. The examiner can normally be reached on M-F from 8:45 a.m. to 4:45 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

D. Saunders:jmr

February 13, 2001

February 14, 2001

David A. Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644